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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/017,718	12/14/2001	Karl H. Weisgraber	UCAL-222	5282

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EXAMINER

TON, THAIAN N

ART UNIT PAPER NUMBER

1632

DATE MAILED: 03/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

**Advisory Action
Before the Filing of an Appeal Brief**

Application No.

10/017,718

Applicant(s)

WEISGRABER ET AL.

Examiner

Thaian N. Ton

Art Unit

1632

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 02 February 2005 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☒ The period for reply expires 5 months from the mailing date of the final rejection.
b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The reply was filed after the date of filing a Notice of Appeal, but prior to the date of filing an appeal brief. The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
(a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
(b) ☐ They raise the issue of new matter (see NOTE below);
(c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
(d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
The status of the claim(s) is (or will be) as follows:
Claim(s) allowed: _____.
Claim(s) objected to: _____.
Claim(s) rejected: 1,3,5,7,14,15 and 20-23.
Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☒ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing of good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because:
See Continuation Sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). _____.
13. ☐ Other: _____.

John W. Tait
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Continuation of 11. does NOT place the application in condition for allowance because: Applicants argue that the instant specification provides ample enablement for the use of the gene-targeted mouse, or a cell isolated therefrom. Applicants point to various places in the specification where methods for using the mouse or cell can be found. See pp. 6-7 of the Response. Applicants argue that the specification provides data that shows that the mouse as instantly claimed produces a modified apoE protein having Arg at a position equivalent to Arg-61 in human ApoE4 and that the Arg-61 ApoE protein produced by the mouse exhibits preferential binding to lower density lipoproteins. See p. 7, 3rd . Further, Applicants point to the Weisgraber Declaration (Exhibit I) to show that the gene-targeted mouse exhibits a degree of neurodegeneration greater than a control mouse. Finally, Applicants argue that the instant specification provides ample enablement for methods of identifying an agent that reduces a phenomenon associated with AD because the instant specification teaches the claimed mouse can be used in such methods, and that these phenomena include neuropathological developments, which include neurodegeneration; consequently, because the Weisgraber Declaration provides evidence that the mice have a degree of neurodegeneration greater than a control mouse, the claimed mice are useful for identifying agents that treat apoE4-related neurodegeneration, such as AD. See p. 8, paragraphs 2-3.

Applicants' arguments have been considered but not found to be persuasive for reasons of record. Firstly, the Weisgraber declaration has not been entered because Applicants have failed to provide good and sufficient reason why this evidence was not presented earlier. See 37 CFR §1.195. The prior rejections of record are maintained because the breadth of the claims fails to enable the claimed mice. In particular, the independent claims (see claim 1, for example) fails to provide an appropriate phenotype such that the claimed mouse could be used in the claimed methods. The mouse, as presented in claim 1 exhibits a phenotype of preferential binding to LDLs. This mouse fails to have a phenotype that would allow it to be used in the method of screening of claim 14. The rejection of record, for enablement of claims 1, 3, 5, 7, 14, 15, 20-22 and newly added claim 23 are maintained for reasons of record.